UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/316,048	05/21/1999	LUC DESGROSEILLERS	10875.77	7290

25545 7590 02/21/2002

GOUDREAU GAGE DUBUC
800 PLACE VICTORIA, SUITE 3400
MONTREAL, QUEBEC, H4Z 1E9
CANADA

EXAMINER	
SHUKLA, RAM R	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 02/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/316,048	DESGROSEILLERS ET AL.	
	Examiner	Art Unit	
	Ram Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

1. Amendment and response filed 11-23-01 have been entered.

2. Claims 1-3 and 9-18 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

3. This application contains claims 1-3 and 9-18 drawn to an invention non-elected with traverse in Paper No. 11. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

4. New claims 24 and 25 have been entered.

5. Claims 4-8 and 19-23 are instantly under consideration.

6. As noted in the previous office action of 8-23-01, applicants have claimed foreign priority based on an application filed in Canada on 5-22-1998, however, a certified copy of the application (#2,238,656) was not filed as required by 35 U.S.C. 119(b) and therefore priority is not granted.

Applicants have stated in their response that they were enclosing a certified copy of the application. Applicants have further stated that the priority document would be hand delivered through their agent Bonini & Kent, however, no such priority document has been received by the office. Accordingly the denial of priority is maintained. Applicants are invited to provide a copy of the post-card or such other document from their agent to indicate that the priority document was delivered to the Patent Office.

7. Submission of a permanent copy of the entire specification including figures is acknowledged.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 4-8 and 19-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO 1, 3, 5, 7, and 9, (ii) an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO 6, SEQ ID NO 11, SEQ ID NO 2, amino acid residues 2-577 of SEQ ID NO 6 and amino acid residues 2-487 of SEQ ID NO 11 and (iii) a nucleic acid complimentary to the full length nucleic acids of (i)-(iii), a recombinant vector comprising the isolated nucleic acid, a method of making a recombinant host cell comprising the isolated nucleic acid, a host comprising the nucleic acid, and a method of making the polypeptide encoded by the nucleic acid, does not reasonably provide enablement for a nucleic acid encoding a Staufen polypeptide comprising amino acids 82-577 or 83-577 of SEQ ID NO 6 or other recited embodiments for reasons of record set forth in the previous office action of 8-23-01 and as discussed below. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 4 recites nucleotides sequences that comprise polynucleotide sequence that are at least 95% identical to nucleotide sequence that encode full length or fragments of the protein of SEQ ID NO 6, aa 82-577 or 83-577 of SEQ ID NO 6, however, it is not clear how would an artisan have known how to use the claimed polynucleotides. According to figure 1B there are four different RNA binding domains (RBD) in the protein, of which RBD1 is present at the N-terminus (amino acid sequences upstream of aa 39) whereas RBD2 is present between AA 62 and 128. RBD3 is present in the middle of the protein whereas RBD4 is present in the C-terminus of the protein. Therefore, a protein containing AA 82-577 and 83-577 would completely lack the RBD1 and part of the RBD 2 (see figure 1B). It is not clear, based on the teachings of the specification, whether these fragments would

bind to dsRNA or would have any other activity attributed to full length SEQ ID NO 6. In other words, it is unclear whether these fragments would have the function of the protein of SEQ ID NO 6. The specification does not how to use a protein that lacked the function of the protein of SEQ ID NO 6. Alternatively, the specification does not teach to how to make the claimed fragments of SEQ ID NO 6 and still maintain the biological activity or function of the wild type protein. It is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence, and the functional properties of the different parts of the protein (see second paragraph in Rudinger J in Peptide Hormones. Editor Parsons JA. Pages 1-7, 1976, University Park Press, Baltimore). Rudinger further add, "The significance of particular amino acids and sequences for different aspects of biological activity can not be predicted *a priori* but must be determined from case to case by painstaking experimental study" (see conclusion on page 6). Similar arguments are valid regarding each of the claimed sequences. If one had to use the claimed nucleotides as a probe, it is not clear whether a probe based on the claimed invention would have resulted in finding a nucleic acid that would encode a protein that would have the function of the protein encoded by the claimed invention. While an artisan may be able to make a deletion mutation in the polynucleotide encoding the amino acid of SEQ ID NO 6 to produce the claimed fragments, an artisan would not know how to assay the activity of such fragments and therefore, the artisan would have to devise a new assay system to study the function of such fragments through extensive experimentation and characterize the claimed polynucleotides and such experimentation would have been undue.

Claim 19 recites nucleic acid molecules comprising a polynucleotide sequence that is at least 95% identical to SEQ ID NO 1, 3, 5, 7, or any sequence that is complimentary to these sequences or a sequence that hybridizes to any of these sequences. It is noted that as currently presented, sequences of claim 19 e would encompass any sequence that is complimentary to SEQ ID NO 1, 3, 5, or 7 which would included the fragments of these sequences. However, the specification does

not teach how to use these fragments, particularly when the fragments may not encode a protein that has the function of the Staufen protein disclosed in the specification. Likewise, regarding claim 19f it is noted that even fragments of SEQ ID NO 1, 3, 5, and 7 would hybridize to these sequences under stringent conditions. For example, Banfi et al teach a 385 bp nucleic acid sequence that has 99.2% sequence similarity with nt 2705-3089 of SEQ ID 1, 3069-3453 of SEQ ID NO 5, and 2911-3295 of SEQ ID NO 7 and therefore the sequence of Banfi et al would be complimentary to the sequence of SEQ ID NO 1, 3, 5 and 7. Furthermore, the sequence of Banfi et al would also hybridize to SEQ ID NO 1, 5, and 7 under stringent conditions. Therefore it would meet the limitation of claim 19e and of 19f. However, the question is: would it encode a protein that functions as a Staufen and there is no guidance in the specification how to use a sequence that hybridized to SEQ ID NO 1, 3, 5, 7 or a sequence that was complimentary to SEQ ID NO 1, 3, 5, or 7 but did not function as Staufen. Regarding the nucleic acids that are 95% identical to the claimed sequences (claims 4, 19, 24, and 25), it is noted that if an artisan did not know how to use the wild type sequence, how would one know how to use sequences that have alterations in the sequences. For example, which 5% sequences of the claimed nucleic acids to alter and whether such alterations would be distributed along the full length of the sequence or concentrated in certain regions. If one had to use sequence that was 95% identical to SEQ ID NO 5, one could change up to about 175 nucleotides since SEQ ID NO 5 consists of 3506 nt and an artisan would not know which 175 nucleotides to change that the resultant encoded protein is still functional. Alternatively, if one had to change only encoding sequences, one could change up to 85 nucleotides, which would translate, into 28 amino acids. Again the specification does not teach which 85 nucleotides could be changed without altering the activity of the encoded protein. If one had to use the claimed nucleotides as a probe, it is not clear whether a probe based on the claimed invention would have resulted in identifying a nucleic acid that would encode a protein that would have the function of the protein encoded by the claimed invention. It is noted that the sequences of the claimed invention were isolated based on sequence similarity with the Drosophila sequence (see example 1),

however, as discussed above there are considerable differences between the human and Drosophila Staufen sequences and the specification does not teach whether they both bind to the same RNA or perform same function. Therefore, based on the sequence similarity data the use of probe for identifying homologous sequences would yield a nucleic acid, which would encode a protein with same function. Again, an artisan would have to go through extensive experimentation to characterize the claimed polynucleotides and such would have been undue. Claim 25d recites a nucleotide sequence encoding conservative substitution of the sequences of 25 a, b and c, however, the specification does not provide any guidance as to what amino acids of SEQ ID NO 2 or 6 were conserved and they could be altered without affecting the activity of the protein. As noted previously by Rudinger et al, "The significance of particular amino acids and sequences for different aspects of biological activity can not be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore an artisan would have required extensive experimentation to determine the amino acids that were conserved and changed one at a time to identify the conserved amino acids and such experimentation would have been undue.

Therefore, in view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use claimed polynucleotides commensurate with the scope of the claimed invention and therefore, limiting the scope of the claimed invention to (i) an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO 1, 3, 5, 7, and 9, (ii) an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO 6, SEQ ID NO 11, SEQ ID NO 2, amino acid residues 2-577 of SEQ ID NO 6 and amino acid residues 2-487 of SEQ ID NO 11 and (iii) a nucleic acid complimentary to the full length nucleic acids of (i)-(iii), a recombinant vector comprising the isolated nucleic acid, a method of making a recombinant host cell comprising the isolated nucleic acid, a host

comprising the nucleic acid, and a method of making the polypeptide encoded by the nucleic acid is proper.

Response to Arguments

Applicant's arguments filed 11-23-01 have been fully considered but they are not persuasive. It is noted that applicants had not responded to all the enablement issues raised in the previous office action. Furthermore, new enablement issues have been raised.

10. Claims 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the revised interim guidelines on written description published January 5, 2001 in the Federal Register, Volume 66, Number 5, page 1099-111 (also available at www.uspto.gov).

When the claims are analyzed in light of the specification, instant invention encompasses claim 19 recites nucleic acid molecules comprising a polynucleotide sequence that is at least 95% identical to SEQ ID NO 1, 3, 5, 7, or any sequence that is complimentary to these sequences or a sequence that hybridizes to any of these sequences. It is noted that as currently presented, sequences of claim 19 e would encompass any sequence that is complimentary to SEQ ID NO 1, 3, 5, or 7 which would included the fragments of these sequences. However, the specification discloses only SEQ ID NO 1, 3, 5, 7, and 9 that encode a polypeptide disclosed in SEQ ID NO 2, 4, 6, 8, and 10. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, SEQ ID Nos 1, 3, 5, and 7 are the only species whose complete structure is disclosed. The specification does not provide any disclosure as to what would have been the sequence structure of the sequence that hybridize to the sequence of SEQ ID NO 1, 3, 5, and 7. Next, then, it is determined whether a representative

number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the only other identifying characteristic is the sequence identity of the claimed polynucleotides with the sequence disclosed in SEQ ID NO 1, 3, 5, and 7. It is noted that the claim as instantly presented would also encompass sequence from any species and the specification does not provide any disclosure whether these sequences from other species would have had same characteristics would have had additional characteristics or properties.

This limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of cDNAs besides SEQ ID NO 1, 3, 5, and 7 that encode the amino acid sequences disclosed in SEQ ID NO 2, 4, 6, and 8 respectively, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

11. Claim 4 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record set forth in the previous office action of 8-23-01.

Response to Arguments

Applicant's arguments filed 11-23-01 have been fully considered but they are not persuasive. Applicants have argued that the sequence of SEQ ID NO 27 was present in the specification and have directed to Figure 1' in line 3 CEL, starting with "mqavf" and ending with "saskt". However, these arguments are not persuasive because SEQ ID NO 27 is a 27 amino acid polypeptide whereas line 3 CEL of figure 1' contains several amino acid residues, therefore it is unclear how SEQ ID NO 27 be the sequence of CEL in figure 1'. Accordingly, the new matter rejection of claim 4 is maintained.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 4-8 and 19-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is indefinite because it recites the term "high stringency condition."

Applicants have argued that an artisan would know what is meant by "highly stringent conditions" and that the specification teaches an example of "high stringency", however these arguments are not persuasive. As noted in the previous office action "high stringency condition" is relative and what would considered high stringent in once situation may not be stringent enough in another condition and therefore nucleic acid molecules isolated under one stringent condition would be completely different from molecules isolated under another stringent condition.

Claim 19 is also indefinite because it is unclear as to what is being claimed in (f) since the claim recites a sequence that hybridizes to the sequence in (f).

Claim 19 is also indefinite it recites "SEQ ID NO:" in line 7 before (e). The placing of this term in line 7 does not make sense.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al (Accession No. AA122533, Database EST, 2-17-97) for reasons of record set forth in the previous office action of 8-23-01.

Response to Arguments

Applicant's arguments filed 11-23-01 have been fully considered but they are not persuasive. Applicants argue that the sequence of Marra et al is in the 3' untranslated region and therefore it does not encompass the claimed invention. However, claim 19 does not have any such limitation that the nucleic acid molecule has to hybridize only to the protein-coding region and therefore, applicant's arguments are not persuasive and the rejection is maintained.

9. Claim 19 is rejected under 35 U.S.C. 102(a) as being anticipated by Banfi et al (Accession No. G30939, Database GenEmbl, 9-29-98; Nature Genetics 13:167-174, 1996) for reasons of record set forth in the previous office action of 11-23-01.

Response to Arguments

Applicant's arguments filed 11-23-01 have been fully considered but they are not persuasive. Applicants argue that the Banfi sequence was accessible only in September 1998 and that the Nature Genetics Article of Banfi does not list this accession no. However, it is noted that they used a clone #22368 for amplifying the cited sequence and the Nature Genetics article lists this clone in table 1. Further Banfi et al teaches that 5' end of the clone# 22368 has homology to the Staufen gene of Drosophila. Therefore, it is clear that the sequence in the accession no G30939 was known at the time of the publication of the article.

10. No claim is allowed.

11. The nucleic acid sequences of SEQ ID NO 1, 3, 5, 7, and 9 are free of the prior art of record.

Applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c) and a copy of all the pending/under consideration claims. For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Kay Pinkney whose telephone number is (703) 305-3553.

Ram R. Shukla, Ph.D.

RAM R. SHUKLA, PH.D
PATENT EXAMINER